REMARKS

Amendments to the Claims

Claims 1, 5, 10 and 20 have been amended without prejudice to make the claims more clear and definite.

Amended claim 1 specifies that the triglyceride fat in a reaction mixture is exposed to a catalyst comprising *Thermomyces lanuginosa* lipase (page 7, lines 6-10, page 2, lines 8-11) having an activity exceeding 250 IUN at the onset of the process (page 6, lines 17-18). Claim 1 also specifies that the process proceeds to a conversion degree on the terminal positions, Re, ranging from 0.3 to less than 0.9 (page 8, lines 32-33). The last limitation recited in claim 1 was also reworded to make the advantage of the process more clear, namely that the conversion degree on the middle position, Ra is greater than a value given by 0.32Re - 0.08.

Amended claim 5 specifies that the catalyst comprises *Thermomyces lanuginosa* (page 7, lines 6-10, page 2, lines 8-11).

Claim 10 has been amended to correct a typographical error (the work "Process" was removed).

Claim 20 was amended to specify that it is the process of exposing the triglyceride fat in the reaction mixture to the catalyst which is carried out by passing the reaction mixture through a packed catalyst bed reactor (this is clear from Example 10).

Claim 20 was also amended to specify that the catalyst comprises *Thermomyces lanuginosa* (page 7, lines 6-10, page 2, lines 8-11 and Example 10).

Claim 7 was amended to recited preferred embodiments that are even further removed from the teachings of the prior art. Specifically, claim 7 specifies that the maximum conversion degree Re to which the process recited in claim 1 is carried out is less than 0.85 (page 8, line 30).

Claim Rejection 35 USC §112

Claims 1-10 and 17-22 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claim 1, the misspelling of *"Thermomyces lanuginosa."* was corrected and amended claim 1 now makes it clear (as expressly stated on page 7, lines 6-10 and all the examples) that the reaction mixture is exposed to a catalyst comprising *Thermomyces lanuginosa* lipase. The specification at page 15, line 10 to page 21, line 9 makes it clear how the enzyme activity of the enzyme catalyst, in IUN units, is determined at the onset of the process.

Regarding claims 2, 4, 17 and 19, amended claim 1 now provides proper antecedent basis for these claims.

Regarding claim 5, the claim has been amended to make it clear that it is the exposure step of the process which is carried out by passing the reaction mixture through a packed catalyst bed reactor, wherein the catalyst comprises *Thermomyces languginosa*.

Regarding claim 10, the typographical error has been corrected to delete the repeat word "Process".

Regarding claim 19, the claim now specifies that the amount of catalyst used when the process is carried out in a batch reactor is 0.05 - 3 wt.% based on the weight of reaction mixture as suggested by the Examiner.

Regarding claim 20, the claim has been rewritten to specify that its is the process of exposing the triglyceride fat in the reaction mixture to the catalyst which is carried out by passing the reaction mixture through a packed catalyst bed reactor and that the catalyst comprises *Thermomyces languginosa*.

In view of the above amendments and remarks, applicants respectfully submit that the metes and bounds recited in the amended claim set are clear and definite and respectfully request that the §112 rejection be reconsidered and withdrawn.

Claim Rejection 35 USC §103

Claims 1-4,6-10,17-19,21, and 22 were rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al. (US 2003/0054509) in light of Sullivan et al. (US 5,391,383) and Zhang et al. (JAOCS. 2001. 78(1): 57-64. Listed on 9/17/07 IDS). Applicants respectfully traverse the rejection.

Statement of Facts

Lee is directed to improving productivity of an enzymatic method for producing transesterified fats by extending the useful life of the enzyme productivity by purifying the substrate oil. (abstract)

Lee is silent about controlling the extent of randomization at the sn-2 position (middle position) of a triglyceride in general and in particular how to effect significant randomization at sn-2 utilizing the sn-1, 3 specific *Thermomyces languginosa* lipase. In fact, Lee is silent about measuring the extent of randomization at any specific position and utilizes the measurement of one or more physical properties of the fats or oils after having contacted the lipase to measure extent of overall reaction (page 6, [0062]).

Lee is silent about enzyme activity (i.e., catalyst) in either "IUN" units or in g/g*h units which are both based on measurement of direct chemical conversion and is silent about any role of enzyme activity at the onset of the process on the extent of randomization at the middle position of a triglyceride.

Sullivan was relied upon by the Examiner for teaching that coconut oil is lauric fat (page 5 – Office Action).

Zhang was relied upon for teaching that Lipozyme TL 1M comprises an immobilized sn-1,3-specific lipase from *Thermomyces lanuginosa* wherein the lipase is silica-granulated. Zhang confirmed the sn-1,3-specificity of this enzyme experimentally (page 63- right column, and table 3).

Zhang, like Lee, is silent concerning any role played by the enzyme activity at the onset of the process in affecting the specificity of the enzyme as measured by the extent of randomization at the middle position of the triglyceride.

Applicants Arguments

Regarding claim 1. Claim 1 is directed to an enzymatic rearrangement process for randomizing fatty acid residues on a triglyceride fat over the terminal and middle positions. Applicants' have discovered that the exposure of triglyceride fat in a reaction mixture which has a water content of 0.001 to 0.1 wt% to a *Thermomyces languginosa* lipase which is known to be an sn-1,3 specific lipase, unexpectedly produces significant rearrangement at the sn-2 position even at relatively low extents of conversion, e.g., less than 90% (less than 85% - claim 7), provided that the enzyme has an *activity of at least 250 IUN* at the *onset of the process*. Under these conditions, the process produces a degree of conversion on the middle position, Ra, which ranges from 0.06-0.75 when the degree of conversion at the terminal positions, Re, ranges from 0.3 to less than 0.9. Under these conditions the process achieves degree of conversion on the middle

position, Ra, which is greater than a minimum value given by 0.32Re - 0.08 (0.32-0.04 – claim 3.

Applicants have found that the fats produced by their process have distinct advantages for food applications including better structuring functionality (page 3, lines 23-28) and significantly lower graininess on storage leading to improved organoleptic properties (example 3, pages 29-31) while maintaining health benefits.

The Examiner admitted that Lee does not teach or suggest that an enzyme *activity of at least 250 IUN* at the *onset of the process* will lead to a significant increase in degree of conversion at the middle position (sn-2) using *Thermomyces languginosa* lipase which is an sn-1,3 specific lipase. However the Examiner asserted that since Lee teaches using the same lipase (Lipozyme TL 1M) that the recited initial enzymatic activity level is rendered obvious (at least 250 IUN, at least 300 IUN, at least 350 IUN; see preceding paragraph), and that various parameters can be altered through routine experimentation to optimize lipase enzymatic activity, the conversion degrees Re and Ra recited in the instant claims.

Thus, the Examiner's argument is based on the supposition that a person of ordinary skill in the art would have expected or recognized that the *specificity* of Lipozyme TL 1M, know to be an sn-1,3 lipase would have changed to allow substantial randomization of fatty acids at the sn-2 position of triglycerides by ensuring that its activity at the *onset of the process* is greater than a threshold value of 250 IUN. Applicants respectfully disagree.

"A particular parameter must first be recognized as a result-effective variable, i.e., a variable which achieves a recognized result, before the determination of the optimum or workable ranges of said variable might be characterized as routine experimentation. *In re Antonie*, 559 F.2d 618, 195 USPQ 6 (CCPA 1977) See MPEP 2144.05.

Nowhere in Lee or Zhang is it taught or suggested that varying the activity of the Lipozyme at the onset of the process will change its *specificity*. The *activity* and *specificity* of an enzyme are completely different attributes. The activity of an enzyme is related to the number of reactions the enzyme will perform under certain standard conditions (i.e. the speed of reaction), whereas the specificity of an enzyme determines which reactions it will perform. Both Lee and Zhang teach that *Thermomyces lanuginosa* lipase is in fact an sn-1,3 specific randomizing lipase (Lee page 1, par 0008, Zhang pages 63 and table 3).

In fact, Zhang concludes that the results "indicates that enzymatically produced margarine fats are different from chemically randomized products. The fatty acids. which are located at the *sn-2* position of starting materials, can be maintained at the position after reaction (page 61, lower right column)".

Lee is concerned entirely with improving the productivity of the lipase, i.e., maintaining the enzyme activity during the reaction. In contrast, applicants have shown in Example 10 that "the sn-2 randomisation (Ra) is not changing when an enzyme catalyst with high starting activity, according to the invention, is as a consequence of the ongoing process functioning at a reduced activity. This proves that the high starting

activity of the enzyme catalyst, as defined in the text, is the key element to the establishment of the sn-2 randomisation (Ra)".

Applicants submit that a person of ordinary skill in the art having Lee and Zhang before him or her would not have expected that substantial randomness at the middle fatty acid (sn-2) of a triglyceride could be introduced using an sn-1,3 specific enzyme especially a conversion degrees in the terminal positions, Re, of less that 0.9, let alone that a change in *specificity* would have required a critical enzyme *activity* at the onset of the process to achieve an Ra greater than a minimum value of 0.32Re – 0.08. That is to say that the onset enzyme activity is not taught as a results effective parameter controlling enzyme sn-2 specificity.

In view of the above amendments and remarks, applicants respectfully request that the §103(a) rejection of claims 1-4, 6-10, 17-19, 21 and 22 rejection over Lee Sullivan and Zhang be reconsidered and withdrawn.

Claims 1-10 and 17-22 were rejected under 35 §U.S.C. 103(a) as being unpatentable over Lee et al., Sullivan et al., and Zhang et al. as applied to claims 1-4, 6-10, 17-19, 21, and 22 above, and further in view of Xu et al. (JAOCS. 2002. 79(6): 561-565. Listed on 9117/07 IDS). Applicants respectfully traverse the rejection.

Statement of Fact

Xu like Lee and Zhang, teaches "Lipozyme TL IM is an sn-1-3 specific lipase from *Thermomyces languginosas* with silica granulation..." (page 561, second column, second to last paragraph).

Xu, like Lee and Zhang, is silent regarding controlling the extent of randomization at the sn-2 position of a triglyceride utilizing the sn-1,3 selective lipase *Thermomyces languginosa*.

Xu like Lee is silent regarding any effect which the specific activity of the enzyme at the onset of the process (I.e., the initial enzyme activity) has on randomization of the Sn-2 fatty acids and in fact does not disclose what the specific activity of the Lipase actually was.

Applicants' Argument

The Examiner relied on Xu for disclosing obtaining various fat products by the lipase-catalyzed modification of oils and fats performed by passing oil through a packed bed reactor of Lipozyme TL 1M. Various flow rates (residence times) were tested to determine their effect on the degree of reaction and the product. Residence times that were tested ranged from about 5 to about 150 minutes.

Xu does not remedy the shortcomings of Lee, Sullivan and Zhang as a prior art reference over claim 1 but instead only reinforces it. Inspection of Table 1 of Xu indicates that under the conditions in which the experiments were carried out, the fatty acid makeup at the sn-2 position of the enzyme treated blend of fish oil and medium chain triglycerides (MCT) was essentially identical to the starting blend indicating essentially no randomization at sn-2. In contrast, chemical esterification achieved essentially complete randomness over the sn-1, sn-2 and sn-3 positions of the triglycerides, i.e., the terminal and middle positions. For example, the untreated mix of fish oil and MCT has a triglycerides composition wherein 0.7% of the sn-2 and 6.9% of

the sn-1,3 contains a 22:5n-3 fatty acid. The Lipozyme treated mixture essentially still contains the same TAG composition: 0.8% of the sn-2 and 7.0% of the sn-1,3 contains a 22:5n-3 fatty. Therefore, almost no sn-2 interesterification has taken place. This becomes especially clear when compared to the chemically interesterified mix wherein 4.9% of the sn-2 and 4.9% of the sn-1,3 contains a 22:5n-3 fatty.

In fact, Xu concludes that it is "obvious that PUFA, especially EPA and DHA, which are mostly located in the sn-2 position in the original fish oil, are maintained in the sn-2 position in the enzymatically interesterified product compared to the randomized one" (page 565, left column, third paragraph).

In contrast, applicants' invention introduces a minimum level of randomization which depends on the conversion degree at the terminal position and is given by

$Ra \geq 0.32Re - 0.08$ (claim 1)
$Ra \geq 0.32Re - 0.04$ (claim 3)

These minimum values are given in the table below and indicate that applicants' method leads to substantial randomization of the middle position, Ra, (at least 5% to around 25%) relative to the terminal position, Re, at levels less than 90% using an enzyme heretofore not known to induce substantial sn-2 randomization. These levels of sn-2 randomization are sufficient to confer formulation and product benefits to triglycerides, e.g., elimination of graininess, treated according to their method without the drawbacks of chemical modification. (Example 7 and 8)

Conversion Degree at terminal positions, Re (sn-1,3)	Minimum Conversion Degree at Middle Position (sn-2)		Minimum Conversion Degree at Middle Position (sn-2)	
	Ra≥0.32Re-0.08	Ra/Re	Ra≥0.32Re-0.04	Ra/Re
30.0%	1.6%	5.3%	5.6%	18.7%
40.0%	4.8%	12.0%	8.8%	22.0%
50.0%	8.0%	16.0%	12.0%	24.0%
60.0%	11.2%	18.7%	15.2%	25.3%
70.0%	14.4%	20.6%	18.4%	26.3%
80.0%	17.6%	22.0%	21.6%	27.0%
85.0%	19.2%	22.6%	23.2%	27.3%
90.0%	20.8%	23.1%	24.8%	27.6%

In summary, applicants submit that a person of ordinary skill in the art would not have sought to routinely experiment with reaction conditions of the *Thermomyces lanuginosa* lipase when trying to find a method of *randomizing fatty acids on all positions*. Applicants submit that based on the teachings of Lee, Zhang and Xu, the artisan would in fact not have used a *Thermomyces lanuginosa* lipase at all but rather would have chosen an alternative nonspecific lipase. Therefore, applicants submit that the fact that they have found novel reaction conditions to perform substantial sn-2 randomization with the *Thermomyces lanuginosa* enzyme which is generally known to be exclusively an sn-1,3 specific enzyme is non-obvious.

In view of the above amendments and remarks, applicants respectfully request that the §103(a) rejection of claims 1-10 and 17-22 over Lee, Sullivan, Zhang and Xu be reconsidered and withdrawn.

Response to Examiner's critique of applicants arguments

In considering applicant's previous arguments the Examiner asserted that

"the features upon which applicant relies (i.e., a lipase which "selectively randomize sn-1 and sn-3 fatty acids" and can "effect significant randomization at the sn-2 position at relatively low extents of conversion by selecting an enzyme activity that is above a threshold value") are not recited in the rejected claims."

Applicants submit that claim 1 recite all of these features. A lipase which *"selectively randomize sn-1 and sn-3 fatty acids" is indeed stated by the limitation " a catalyst comprising Thermomyces lanuginosa* lipase" because this enzyme is know to selectively randomize only sn-1 and sn-3 fatty acids. The feature "*effect significant randomization at the sn-2 position"* is recited by the phrase "randomizing fatty acid residues on a triglyceride fat over the terminal and middle positions", the feature "*at relatively low extents of conversion"* is recited in claim 1 as "Re, ranging from 0.3 to less than 0.9". The feature "*selecting an enzyme activity that is above a threshold value*" is recited in claim 1 as "having an activity of at least 250 IUN".

Furthermore, the Examiner stated *'In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based on hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from applicant's disclosure, such a reconstruction is proper."*

Applicants submit that the knowledge that certain reaction conditions allow the otherwise sn-1,3 specific lipase, *Thermomyces lanuginosa*, to become able to

randomize fatty acids at the sn-2 position is knowledge gleaned only from applicant's disclosure and was not publicly available at the time the invention was made.

In view of the above amendments and remarks, applicants respectfully request that the 103(a) rejection over Lee, Sullivan, Zhang and Xu be reconsidered and withdrawn and that the application be allowed to issue.

If a telephone conversation would be of assistance in advancing prosecution of the subject application, applicants' undersigned agent invites the Examiner to telephone him at the number provided.

Respectfully submitted,

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